

[0290] We claim:

1. A mutant Bik polypeptide comprising anti-cell proliferative activity, pro-apoptotic activity, or both.
2. The polypeptide of claim 1, wherein the anti-cell proliferative activity, the pro-apoptotic activity, or both of the polypeptide is substantially the same or more effective than native Bik polypeptide.
3. The polypeptide of claim 1, wherein the mutant Bik polypeptide comprises at least one amino acid substitution.
4. The polypeptide of claim 3, wherein the substitution prevents phosphorylation of the Bik polypeptide under conditions that would result in phosphorylation of an unsubstituted Bik polypeptide.
5. The polypeptide of claim 4, wherein the amino acid substitution is at Thr³³, Ser³⁵, or both Thr³³ and Ser³⁵.
6. The polypeptide of claim 5, wherein the substitution is a Thr³³ to Asp³³ substitution.
7. The polypeptide of claim 5, wherein the substitution is a Ser³⁵ to Asp³⁵ substitution.
8. The polypeptide of claim 5, wherein the substitution is a Thr³³ to Asp³³ substitution, a Ser³⁵ to Asp³⁵ substitution, or both.
9. The polypeptide of claim 1, further defined as a composition in a pharmacologically acceptable excipient in which the Bik polypeptide is dispersed.
10. The polypeptide of claim 1, further defined as comprised in a pharmacologically acceptable excipient.

11. The polypeptide of claim 1, further defined as being comprised in a suitable container in a kit.
12. A method comprising administering to a cell a Bik polypeptide having an amino acid substitution.
13. The method of claim 12, wherein the amino acid substitution is at Thr³³, Ser³⁵, or both Thr³³ and Ser³⁵.
14. The method of claim 13, wherein the substitution is a Thr³³ to Asp³³ substitution.
15. The method of claim 13, wherein the substitution is a Ser³⁵ to Asp³⁵ substitution.
16. The method of claim 12, wherein the polypeptide further comprises a protein transduction domain.
17. The method of claim 12, wherein the cell is comprised in an animal.
18. The method of claim 17, wherein the animal is a human.
19. The method of claim 18, wherein the human has a proliferative cell disorder.
20. The method of claim 19, wherein the proliferative cell disorder is cancer.
21. The method of claim 20, wherein the cancer is breast cancer, prostate cancer, ovarian cancer, sarcoma, lung cancer, brain cancer, pancreatic cancer, liver cancer, bladder cancer, gastrointestinal cancer, leukemia, lymphoma, or myeloma.
22. The method of claim 20, wherein the cancer is estrogen receptor positive, is EGF receptor overexpressing, is *Her2/neu*-overexpressing, is not *Her-2/neu*-overexpressing, is Akt overexpressing, is angrogen independent, or is androgen dependent.

23. The method of claim 20, wherein the cancer is a solid tumors, such as, for example, sarcoma, lung, brain, pancreatic, liver, bladder, gastrointestinal cancers, or hematologic malignancies, such as leukemia, lymphoma, and myeloma
24. The method of claim 20, wherein the proliferative cell disorder is restenosis.
25. The method of claim 12, wherein the polypeptide is comprised in pharmacologically acceptable excipient.
26. The method of claim 25, wherein the polypeptide is complexed with a lipid.
27. The method of claim 13, wherein administering to the cell a Bik polypeptide having an amino acid substitution at Thr³³ comprises administering to the individual a nucleic acid encoding a Bik polypeptide having an amino acid substitution at Thr³³.
28. The method of claim 27, wherein the expression of the nucleic acid is regulated by a tissue-specific control sequence.
29. The method of claim 27, wherein the nucleic acid is comprised in a plasmid, a retroviral vector, an adenoviral vector, an adeno-associated viral vector, or a liposome.
30. The method of claim 27, wherein the nucleic acid is dispersed in a pharmacologically acceptable excipient.
31. The method of claim 28, wherein the tissue-specific control sequence is a breast cancer-specific control sequence.
32. The method of claim 28, wherein the tissue-specific control sequence is a prostate cancer-specific control sequence.
33. The method of claim 28, wherein the tissue-specific control sequence is a pancreatic cancer-specific control sequence.

34. The method of claim 13, wherein administering to the cell a Bik polypeptide having an amino acid substitution at Ser³⁵ comprises administering to the individual a nucleic acid encoding a Bik polypeptide having an amino acid substitution at Ser³⁵.
35. The method of claim 34, wherein the expression of the nucleic acid is regulated by a tissue-specific control sequence.
36. The method of claim 34, wherein the nucleic acid is comprised in a plasmid, a retroviral vector, an adenoviral vector, an adeno-associated viral vector, or a liposome.
37. The method of claim 34, wherein the nucleic acid is dispersed in a pharmacologically acceptable excipient.
38. The method of claim 35, wherein the tissue-specific control sequence is a breast cancer-specific control sequence.
39. The method of claim 35, wherein the tissue-specific control sequence is a prostate cancer-specific control sequence.
40. The method of claim 35, wherein the tissue-specific control sequence is a pancreatic cancer-specific control sequence.
41. The method of claim 12, further defined as a method of preventing growth of a cell in an individual.
42. The method of claim 13, further defined as comprising modifying the Bik polypeptide at amino acid position 33, amino acid position 35, or both, wherein the modification results in an inability of the amino acid to be phosphorylated.
43. A method of inhibiting cell proliferation comprising contacting a cell with a mutant Bik polypeptide in an amount effective to inhibit the cell proliferation.

44. The method of claim 43, wherein the mutant Bik polypeptide is further defined as having anti-cell proliferative activity, pro-apoptotic activity, or both.
45. The method of claim 44, wherein the anti-cell proliferative activity, the pro-apoptotic activity, or both of the polypeptide is substantially the same or more effective than native Bik polypeptide.
46. The method of claim 43, wherein the mutant Bik comprises an amino acid substitution.
47. The method of claim 46, wherein the substitution in the mutant Bik polypeptide prevents phosphorylation of the Bik polypeptide under conditions that would result in phosphorylation of an unsubstituted Bik polypeptide.
48. The method of claim 47, wherein the amino acid substitution is at Thr³³, Ser³⁵, or both Thr³³ and Ser³⁵.
49. The method of claim 48, wherein the substitution is a Thr³³ to Asp³³ substitution.
50. The method of claim 48, wherein the substitution is a Ser³⁵ to Asp³⁵ substitution.
51. A method of treating a proliferative cell disorder in an individual comprising the step of administering to the individual a mutant Bik composition.
52. The method of claim 51, wherein the mutant Bik polypeptide is further defined as having anti-cell proliferative activity, pro-apoptotic activity, or both.
53. The method of claim 51, wherein the anti-cell proliferative activity, the pro-apoptotic activity, or both of the polypeptide is substantially the same or more effective than native Bik polypeptide.

54. The method of claim 51, wherein the mutant Bik comprises an amino acid substitution.
55. The method of claim 54, wherein the substitution is at Thr³³, Ser³⁵, or both Thr³³ and Ser³⁵.
56. The method of claim 54, wherein the amino acid substitution in the mutant Bik polypeptide prevents phosphorylation of the Bik polypeptide under conditions that would result in phosphorylation of an unsubstituted Bik polypeptide.
57. The method of claim 54, wherein the substitution is a Thr³³ to Asp³³ substitution.
58. The method of claim 54, wherein the substitution is a Ser³⁵ to Asp³⁵ substitution.
59. A method of treating cancer in an individual having the cancer, comprising contacting at least one cancer cell of the individual with a therapeutically effective amount of a polynucleotide encoding a Bik polypeptide having a Thr³³ to Asp³³ substitution, a Ser³⁵ to Asp³⁵ substitution, or both, wherein the polynucleotide is comprised in an liposome.
60. The method of claim 59, wherein the expression of the polynucleotide encoding the mutant Bik polypeptide is regulated by a tissue-specific control sequence.
61. The method of claim 60, wherein the tissue-specific control sequence is a breast cancer-specific control sequence.
62. The method of claim 60, wherein the tissue-specific control sequence is a prostate cancer-specific control sequence.
63. The method of claim 60, wherein the tissue-specific control sequence is a pancreatic cancer-specific control sequence.

64. A polynucleotide construct comprising nucleic acid sequence encoding a mutant Bik polypeptide.
65. The polynucleotide of claim 64, wherein the construct further comprises a tissue-specific control sequence operatively linked to the sequence encoding the mutant Bik polypeptide.
66. The polynucleotide of claim 65, wherein the tissue-specific control sequence comprises a breast cancer-specific control sequence, a prostate cancer-specific control sequence, or a pancreatic cancer-specific control sequence.
67. The polynucleotide of claim 65, wherein the tissue-specific control sequence comprises a breast cancer-specific control sequence.
68. The polynucleotide of claim 65, wherein the tissue-specific control sequence comprises a prostate cancer-specific control sequence.
69. The polynucleotide of claim 65, wherein the tissue-specific control sequence comprises a pancreatic cancer-specific control sequence.
70. The polynucleotide of claim 64, wherein the mutant Bik polypeptide comprises a Thr³³ to Asp³³ substitution, a Ser³⁵ to Asp³⁵ substitution, or both.
71. The polynucleotide of claim 64, further defined as being comprised in a liposome.
72. A method of sensitizing a tumor cell to a chemotherapeutic agent, comprising delivering to the cell a mutant Bik composition.
73. The method of claim 72, wherein sensitizing the tumor cell to the chemotherapeutic agent is further defined as enhancing chemotherapeutic agent-induced apoptosis of the cell.
74. The method of claim 72, wherein the mutant Bik composition is further defined as a mutant Bik polypeptide.

75. The method of claim 72, wherein the mutant Bik composition is further defined as a polynucleotide encoding a mutant Bik polypeptide.